machines. All results are shown in various graphical representations to provide better visibility of the underlying patterns. Other display tools include scatterplot displays of expression measurements and histograms of various expression ratio frequencies.

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=> d his

     (FILE 'HOME' ENTERED AT 12:43:58 ON 19 MAR 2004)

     FILE 'MEDLINE, BIOSIS' ENTERED AT 12:47:08 ON 19 MAR 2004
L1          687 S EXPRESSION AND PRINCIPAL COMPONENT
L2          283 S GENE EXPRESSION AND PRINCIPAL COMPONENT
L3           69 S L2 AND PY<2001
L4           51 DUPLICATE REMOVE L3 (18 DUPLICATES REMOVED)

=> s gene expression and pricipal component analysis
L5            0 GENE EXPRESSION AND PRICIPAL COMPONENT ANALYSIS

=> s gene expression and principal component analysis
L6          202 GENE EXPRESSION AND PRINCIPAL COMPONENT ANALYSIS

=> s l6 and py<2000
L7           13 L6 AND PY<2000

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8            8 DUPLICATE REMOVE L7 (5 DUPLICATES REMOVED)

=> d 1-8 bib ab

L8   ANSWER 1 OF 8     MEDLINE on STN                    DUPLICATE 1
AN   1999168493     MEDLINE
DN   PubMed ID: 10070945
TI   Statistical analysis of array expression data as applied to the problem of
     tamoxifen resistance.
CM   Comment in: J Natl Cancer Inst. 1999 Mar 3;91(5):400-1. PubMed ID:
     10070933
AU   Hilsenbeck S G; Friedrichs W E; Schiff R; O'Connell P; Hansen R K; Osborne
     C K; Fuqua S A
CS   Department of Medicine, The University of Texas Health Science Center, San
     Antonio 78248-7884, USA.
NC   CA30195 (NCI)
     CA54174 (NCI)
     CA58183 (NCI)
SO   Journal of the National Cancer Institute, (1999 Mar 3) 91 (5)
     453-9.
     Journal code: 7503089. ISSN: 0027-8874.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199903
ED   Entered STN: 19990326
     Last Updated on STN: 19990326
     Entered Medline: 19990317
AB   BACKGROUND: Although the emerging complementary DNA (cDNA) array
     technology holds great promise to discern complex patterns of gene
     expression, its novelty means that there are no well-established
     standards to guide analysis and interpretation of the data that it
```

produces. We have used preliminary data generated with the CLONTECH Atlas human cDNA array to develop a practical approach to the statistical analysis of these data by studying changes in **gene expression** during the development of acquired tamoxifen resistance in breast cancer. METHODS: For hybridization to the array, we prepared RNA from MCF-7 human breast cell tumors, isolated from our athymic nude mouse xenograft model of acquired tamoxifen resistance during estrogen-stimulated, tamoxifen-sensitive, and tamoxifen-resistant growth. **Principal components analysis** was used to identify genes with altered expression. RESULTS AND CONCLUSIONS: **Principal components analysis** yielded three principal components that are interpreted as 1) the average level of **gene expression**, 2) the difference between estrogen-stimulated **gene expression** and the average of tamoxifen-sensitive and tamoxifen-resistant **gene expression**, and 3) the difference between tamoxifen-sensitive and tamoxifen-resistant **gene expression**. A bivariate (second and third principal components) 99% prediction region was used to identify outlier genes that exhibit altered expression. Two representative outlier genes, erk-2 and HSF-1 (heat shock transcription factor-1), were chosen for confirmatory study, and their predicted relative expression levels were confirmed in western blot analysis, suggesting that semiquantitative estimates are possible with array technology. IMPLICATIONS: **Principal components analysis** provides a useful and practical method to analyze **gene expression** data from a cDNA array. The method can identify broad patterns of expression alteration and, based on a small simulation study, will likely provide reasonable power to detect moderate-sized alterations in clinically relevant genes.

L8 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:86733 BIOSIS
DN PREV200000086733
TI Phylogeny and diversity of Bradyrhizobium strains isolated from the root nodules of peanut (Arachis hypogaea) in Sichuan, China.
AU Zhang, Xiaoping [Reprint author]; Nick, Giselle [Reprint author]; Kaijalainen, Seppo [Reprint author]; Terefework, Zewdu [Reprint author]; Paulin, Lars; Tighe, Scott W.; Graham, Peter H.; Lindstrom, Kristina [Reprint author]
CS Department of Applied Chemistry and Microbiology, Biocenter 1, University of Helsinki, Helsinki, Finland
SO Systematic and Applied Microbiology, (Sept., 1999) Vol. 22, No. 3, pp. 378-386. print.
CODEN: SAMIDF. ISSN: 0723-2020.
DT Article
LA English
ED Entered STN: 1 Mar 2000
Last Updated on STN: 3 Jan 2002
AB Twenty-two rhizobial strains isolated from the root nodules of two Chinese peanut cultivars (Arachis hypogaea L. Tianfu no. 3 and a local cultivar) growing at four different sites in the Sichuan province, Southwest China, were characterized by growth rate, rep-PCR, PCR-RFLP of 16S rDNA, partial sequencing of ribosomal genes, and fatty acid - methyl ester analysis (FAME), and compared with strains representing Bradyrhizobium japanicum, B. elkanii and other unclassified Bradyrhizobium sp. All peanut isolates from Sichuan were bradyrhizobia. Dendrograms constructed using the rep-PCR fingerprints grouped the strains mainly according to their geographic and cultivar origin. Based on PCR-RFLP and partial sequence analysis of 16S rDNA it appears that peanut bradyrhizobial strains from Sichuan are similar to peanut strains from Africa and Israel, and closely related to B. japonicum. In contrast, analysis of FAME data using two-dimensional **principal component analysis**

indicated that Bradyrhizobium sp. (Arachis) were similar to, but slightly different from other bradyrhizobia. The presence and level of fatty acid 16:1 w5c was the distinguishing feature. The results of PCR-RFLP of the 16S rRNA gene, the partial sequence analysis of 16S rDNA, and FAME were in good agreement.

L8 ANSWER 3 OF 8 MEDLINE on STN
AN 1998171572 MEDLINE
DN PubMed ID: 9502826
TI Corticosteroid regulation of ion channel conductances and mRNA levels in individual hippocampal CA1 neurons.
AU Nair S M; Werkman T R; Craig J; Finnell R; Joels M; Eberwine J H
CS Department of Pharmacology, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania 19104, USA.
NC AG9900 (NIA)
SO Journal of neuroscience : official journal of the Society for Neuroscience, **(1998 Apr 1)** 18 (7) 2685-96.
Journal code: 8102140. ISSN: 0270-6474.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980416
Last Updated on STN: 19980416
Entered Medline: 19980407
AB Overexposure to corticosteroid hormones is harmful to hippocampal neuronal integrity, likely by perturbation of calcium homeostasis. To identify molecular mechanisms at the single-cell level, we characterized mRNA expression corresponding to voltage- and ligand-gated Ca channels in individual dissociated CA1 neurons in response to long-term corticosterone (CORT) exposure. Predominant mineralocorticoid receptor occupation (ADC-LO group) resulted in low levels of P/Q- and L-type Ca channel mRNAs, high levels of GluR-2 versus GluR-1, and a high ratio of NMDAR-2A to NMDAR-2B mRNA. Corresponding alterations in protein expression were consistent with the restriction of Ca influx. In contrast, additional glucocorticoid receptor occupation (ADC-HI group) altered the expression of these mRNAs in a manner consistent with enhanced Ca influx; interestingly, qualitatively similar alterations were seen in control ADX neurons. Electrophysiological data from the same neurons indicate that Ca current amplitudes also are modulated by CORT, although on a shorter time scale. Finally, **principal components analysis** (PCA) suggests that neuronal AMPA and NMDA receptor composition may be regulated by MR and GR activation in a complex manner. Therefore, our data implicate molecular events by which CORT may regulate Ca influx into CA1 hippocampal neurons.

L8 ANSWER 4 OF 8 MEDLINE on STN DUPLICATE 2
AN 97312646 MEDLINE
DN PubMed ID: 9169087
TI Developmental expression of morphoregulatory genes in the mouse embryo: an analytical approach using a novel technology.
AU Craig J C; Eberwine J H; Calvin J A; Wlodarczyk B; Bennett G D; Finnell R H
CS Department of Veterinary Anatomy and Public Health, Texas A&M University, College Station 77843, USA.
NC DE 11303 (NIDCR)
ES 07165 (NIEHS)
SO Biochemical and molecular medicine, **(1997 Apr)** 60 (2) 81-91.
Journal code: 9508702. ISSN: 1077-3150.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199707
ED Entered STN: 19970721
Last Updated on STN: 20000303
Entered Medline: 19970707
AB The molecular techniques of in situ transcription and antisense RNA amplification (IST/aRNA) have allowed for the monitoring of coordinate changes in the expression of multiple genes simultaneously. However, the analysis of their concurrent behavior during murine embryogenesis has been problematic. Studies involving the investigation of temporal and spatial **gene expression** during embryogenesis have focused solely on the analysis of isolated, single gene events. Such an approach has failed to provide an integrative picture of genetic control over the varied and complicated cellular processes governing embryogenesis. In order to interpret the enormous amount of **gene expression** data generated by these procedures, we have attempted to develop an analytical framework by employing the statistical concepts of **principal components analysis** (PCA). For the current study, we performed IST/aRNA on neural tubes dissected from the highly inbred LM/Bc murine strain collected during four gestational time periods. A subset of these genes, representing a partial signaling pathway in the developing neuroepithelium, was then subjected to PCA. Here, we report that PCA highlighted the transcriptional interplay among the genes p53, wee-1, Tgf beta-2, and bcl-2 such that the combined reciprocal regulation of their gene products is suggestive of a predominant proliferative state for the developing neuroepithelium. The application of PCA to the **gene expression** data has elucidated previously unknown interrelationships among cell cycle genes, growth, and transcription factors on a transcriptional level during critical stages of neurulation. The information gleaned from this analysis, while not definitive, suggests distinct hypotheses to guide future research.

L8 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 3
AN 96423283 MEDLINE
DN PubMed ID: 8825884
TI Adult fragile X syndrome: neuropsychology, brain anatomy, and metabolism.
AU Schapiro M B; Murphy D G; Hagerman R J; Azari N P; Alexander G E; Miezejeski C M; Hinton V J; Horwitz B; Haxby J V; Kumar A; +
CS Section on Brain Aging and Dementia, National Institute on Aging, Clinical Center, Bethesda, Maryland 20892, USA.
SO American journal of medical genetics, **(1995 Dec 18)** 60 (6) 480-93.
Journal code: 7708900. ISSN: 0148-7299.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961205
AB To understand the implications of suboptimal **gene expression** in fragile X syndrome -fra(X)-, we sought to define the central nervous abnormalities in fra(X) syndrome to determine if abnormalities in specific brain regions or networks might explain the cognitive and behavioral abnormalities in this syndrome. Cranial and ventricular volumes were measured with quantitative computed tomography (CT), regional cerebral metabolic rates for glucose (rCMRglc) were measured with [18-F]-2-fluoro-2-deoxy-D-glucose (18FDG), and patterns of cognition were determined with neuropsychological testing in ten healthy,

male patients with karyotypically proven fra(X) syndrome (age range 20-30 yr). Controls for the CT studies were 20 healthy males (age range 21-37 yr), controls for the PET studies were 9 healthy males (age range 22-31 yr), and controls for the neuropsychological tests were 10 young adult, male Down syndrome (DS) subjects (age range 22-31 yr). The mean mental age of the fra(X) syndrome group was 5.3 yr (range 3.5-7.5 yr; Stanford-Binet Intelligence Scale). Despite comparable levels of mental retardation, the fra(X) subjects showed poorer attention/short term memory in comparison to the DS group. Further, the fra(X) subjects showed a relative strength in verbal compared to visuospatial attention/short term memory. As measured with quantitative CT, 8 fra(X) subjects had a significant ($P < 0.05$) 12% greater intracranial volume (1,410 +/- 86 cm3) as compared to controls (1,254 +/- 122 cm3). Volumes of the right and left lateral ventricles and the third ventricle did not differ between groups. Seven of eight patients had greater right lateral ventricle volumes than left, as opposed to 9 out of 20 controls ($P < 0.05$). Global gray matter CMR-glc in nine fra(X) patients was 9.79 +/- 1.28 mg/100 g/minute and did not differ from 8.84 +/- 1.31 mg/100 g/minute in the controls. R/L asymmetry in metabolism of the superior parietal lobe was significantly higher in the patients than controls. A preliminary **principal component analysis** of metabolic data showed that the fra(X) subjects tended to form a separate subgroup that is characterized by relative elevation of normalized metabolism in the lenticular nucleus, thalamus, and premotor regions. Further, a discriminant function, that reflected rCMRglc interactions of the right lenticular and left premotor regions, distinguished the fra(X) subjects from controls. These regions are part of a major group of functionally and anatomically related brain regions and appear disturbed as well in autism with which fra(X) has distinct behavioral similarities. These results show a cognitive profile in fra(X) syndrome that is distinct from that of Down syndrome, that the larger brains in fragile X syndrome are not accompanied by generalized cerebral cortical atrophy or hypoplasia, and that distinctive alterations in resting regional glucose metabolism, measured with 18 FDG and PET, occur in fra(X) syndrome.

L8 ANSWER 6 OF 8 MEDLINE on STN DUPLICATE 4
AN 95058153 MEDLINE
DN PubMed ID: 7968492
TI Evolution of codon usage and base contents in kinetoplastid protozoans.
AU Alvarez F; Robello C; Vignali M
CS Departamento de Genetica, Facultad de Medicina, Montevideo, Uruguay.
SO Molecular biology and evolution, **(1994 Sep)** 11 (5) 790-802.
Journal code: 8501455. ISSN: 0737-4038.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199412
ED Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941202
AB In this study we analyze and compare the trends in codon usage in five representative species of kinetoplastid protozoans (Crithidia fasciculata, Leishmania donovani, L. major, Trypanosoma cruzi and T. brucei), with the purpose of investigating the processes underlying these trends. A **principal component analysis** shows that the G+C content at the third codon position represents the main source of codon-usage variation, both within species (among genes) and among species. The non-Trypanosoma species exhibit narrow distributions in codon usage, while both Trypanosoma species present large within-species heterogeneity. The three non-Trypanosoma species have very similar codon-usage preferences. These codon preferences are also shared by the

highly expressed genes of T. cruzi and to a lesser degree by those of T. brucei. This leads to the conclusion that the codon preferences shared by these species are the ancestral ones in the kinetoplastids. On the other hand, the study of noncoding sequences shows that Trypanosoma species exhibit mutational biases toward A + T richness, while the non-Trypanosoma species present mutational pressure in the opposite direction. These data taken together allow us to infer the origin of the different codon-usage distributions observed in the five species studied. In C. fasciculata and Leishmania, both mutational biases and (translational) selection pull toward G + C richness, resulting in a narrow distribution. In Trypanosoma species the mutational pressure toward A + T richness produced a shift in their genomes that differentially affected coding and noncoding sequences. The effect of these pressures on the third codon position of genes seems to have been inversely proportional to the level of **gene expression.**

L8 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 5
AN 92007699 MEDLINE
DN PubMed ID: 1915248
TI Global analysis of lymphocyte **gene expression:** perturbation of H-9 cells by infection with distinct isolates of human immunodeficiency virus--an exposition by multivariate analysis of a host-parasite interface.
AU Kettman J R; Robinson R A; Kuhn L; Lefkovits I
CS Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75239-9048.
NC AI 11851 (NIAID)
SO Electrophoresis, **(1991 Jul-Aug)** 12 (7-8) 554-69.
Journal code: 8204476. ISSN: 0173-0835.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199111
ED Entered STN: 19920124
Last Updated on STN: 19970203
Entered Medline: 19911107
AB AIDS is a progressive disease associated with steady loss of helper T cells and several other functions. As the disease evolves, cytopathogenic human immunodeficiency (HIV) variants of increasing virulence can be isolated from the host. The HIV is an unusually variable genome by virtue of a low replication fidelity. In this report we describe our effort to test the hypothesis that there is a correlation between virus variability and cytopathogenicity, and further, that there is an "impact" of the virus infection on the expression of host cellular genes. To search for such a relationship, we infected H-9 cells (human CD4+ lymphoblastoid cell line) with each of 5 isolates of HIV of distinct origin and cytopathogenicity. To measure the influence of the virus infection on the expression of host cellular genes, shortly after infection, (3 h or 13 h), cells were radiolabeled and the radioactive polypeptides separated by two-dimensional gel electrophoresis. Radiofluorographs were prepared and analyzed to determine relative rates of biosynthesis of cellular polypeptides. To organize the large amounts of data found, cluster analysis and **principal component analysis** were used to expose the data in formats that allowed a model construction. The rates of biosynthesis of many cellular polypeptides were altered upon viral infection in terms of both enhancements and impairment of biosynthesis. Some of the variation in polypeptide synthesis was isolate-specific, while most alterations were of modest magnitude. There appears to be no "overall effect" associated with infection by a cytopathic variant of the virus. Polypeptides affected by the cytopathic variants were determined as targets for further investigation. The method used promotes the

measurement of "ensemble" information that is characteristic of the process and it promotes the creation of models of virus action.

L8 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1994:257797 BIOSIS
DN PREV199497270797
TI The genetics and cost of chemical defense in the two-spot ladybird (Adalia bipunctata L.).
AU Holloway, Graham J. [Reprint author]; De Jong, Peter W.; Ottenheim, Mart
CS Dep. Pure Applied Zool., AMS Building, Univ. Reading, Whiteknights, P.O. Box 228, Reading, Berkshhire RG6 2AJ, UK
SO Evolution, (1993 (1994)) Vol. 47, No. 4, pp. 1229-1239. .
CODEN: EVOLAO. ISSN: 0014-3820.
DT Article
LA English
ED Entered STN: 8 Jun 1994
Last Updated on STN: 8 Jun 1994
AB Ladybirds (Coccinellidae) defend themselves against attack by vertebrate predators by exuding a fluid from the femero-tibial joints. This fluid carries a noxious or toxic alkaloid. The amount of fluid produced during a single attack can be very high (up to 20% of fresh body weight), and the weight of the self-synthesized alkaloid can amount to several percent of the weight of the fluid. A study was carried out on these two defense characters and two other fitness characters (body weight and growth rate) to demonstrate a cost to defense in the form of genetic trade-offs between characters. The two sexes were analyzed separately, and a jackknife procedure was used to attach errors to the estimates of V-a and cov-a. All four characters were associated with high levels of V-a, but the cov-a values were mixed, some being negative and others positive. **Principal-component analysis** indicated the operation of factors constraining the cov-a values in males, and further possible reasons for the appearance of so many positive values are explored. A matrix analysis showed that the genetic variance/covariance matrices of the two sexes were significantly different from each other. Breeding values derived from sons plotted on breeding values from daughters had correlation coefficients significantly less than + 1. This finding indicated that a substantial amount of sex-dependent **gene expression** was occurring.

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=> LOG Y

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FULL ESTIMATED COST	24.30	25.35

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PASSWORD:
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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09   CA/CAplus records now contain indexing from 1907 to the
                   present
 NEWS  4  DEC 08   INPADOC: Legal Status data reloaded
 NEWS  5  SEP 29   DISSABS now available on STN
 NEWS  6  OCT 10   PCTFULL: Two new display fields added
 NEWS  7  OCT 21   BIOSIS file reloaded and enhanced
 NEWS  8  OCT 28   BIOSIS file segment of TOXCENTER reloaded and enhanced
 NEWS  9  NOV 24   MSDS-CCOHS file reloaded
 NEWS 10  DEC 08   CABA reloaded with left truncation
 NEWS 11  DEC 08   IMS file names changed
 NEWS 12  DEC 09   Experimental property data collected by CAS now available
                   in REGISTRY
 NEWS 13  DEC 09   STN Entry Date available for display in REGISTRY and CA/CAplus
 NEWS 14  DEC 17   DGENE: Two new display fields added
 NEWS 15  DEC 18   BIOTECHNO no longer updated
 NEWS 16  DEC 19   CROPU no longer updated; subscriber discount no longer
                   available
 NEWS 17  DEC 22   Additional INPI reactions and pre-1907 documents added to CAS
                   databases
 NEWS 18  DEC 22   IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
 NEWS 19  DEC 22   ABI-INFORM now available on STN
 NEWS 20  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS 21  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus
 NEWS 22  FEB 05   German (DE) application and patent publication number format
                   changes
 NEWS 23  MAR 03   MEDLINE and LMEDLINE reloaded
 NEWS 24  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS 25  MAR 03   FRANCEPAT now available on STN

 NEWS EXPRESS  MARCH 5 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004
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 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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FILE 'HOME' ENTERED AT 18:05:15 ON 19 MAR 2004

=> file .pub
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 18:05:24 ON 19 MAR 2004

FILE 'BIOSIS' ENTERED AT 18:05:24 ON 19 MAR 2004
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=> s (ccl4 or carbon tetrachloride) and (toxic? or hepatitis)
L1 9416 (CCL4 OR CARBON TETRACHLORIDE) AND (TOXIC? OR HEPATITIS)

=> s l1 and (gene expression or microarray)
L2 181 L1 AND (GENE EXPRESSION OR MICROARRAY)

=> s l2 and py<2000
L3 105 L2 AND PY<2000

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 85 DUPLICATE REMOVE L3 (20 DUPLICATES REMOVED)

=> d 1-10 bib ab

L4 ANSWER 1 OF 85 MEDLINE on STN
AN 1999261907 MEDLINE
DN PubMed ID: 10330021
TI Acute **carbon tetrachloride** feeding induces damage of large but not small cholangiocytes from BDL rat liver.
AU LeSage G D; Glaser S S; Marucci L; Benedetti A; Phinizy J L; Rodgers R; Caligiuri A; Papa E; Tretjak Z; Jezequel A M; Holcomb L A; Alpini G
CS Department of Internal Medicine, Scott & White Hospital and The Texas A&M University System Health Science Center College of Medicine, Temple, Texas 76504, USA.
SO American journal of physiology, **(1999 May)** 276 (5 Pt 1) G1289-301.
Journal code: 0370511. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990607
AB Bile duct damage and/or loss is limited to a range of duct sizes in cholangiopathies. We tested the hypothesis that **CCl4** damages only large ducts. **CCl4** or mineral oil was given to bile duct-ligated (BDL) rats, and 1, 2, and 7 days later small and large cholangiocytes were purified and evaluated for apoptosis, proliferation, and secretion. In situ, we measured apoptosis by morphometric and TUNEL analysis and the number of small and large ducts by morphometry. Two days after **CCl4** administration, we found an increased number of small

ducts and reduced number of large ducts. In vitro apoptosis was observed only in large cholangiocytes, and this was accompanied by loss of proliferation and secretion in large cholangiocytes and loss of choleretic effect of secretin. Small cholangiocytes de novo express the secretin receptor gene and secretin-induced cAMP response. Consistent with damage of large ducts, we detected cytochrome P-4502E1 (which **CCl4** converts to its radicals) only in large cholangiocytes. **CCl4** induces selective apoptosis of large ducts associated with loss of large cholangiocyte proliferation and secretion.

L4 ANSWER 2 OF 85 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:320667 BIOSIS
DN PREV199900320667
TI Microsomal ethanol-oxidizing system (MEOS): The first 30 years (1968-1998)-A review.
AU Lieber, Charles S. [Reprint author]
CS Bronx VA Medical Center (151-2), 130 West Kingsbridge Rd., Bronx, NY, 10468, USA
SO Alcoholism Clinical and Experimental Research, (June, 1999) Vol. 23, No. 6, pp. 991-1007. print.
CODEN: ACRSDM. ISSN: 0145-6008.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 17 Aug 1999
Last Updated on STN: 17 Aug 1999
AB Oxidation of ethanol via alcohol dehydrogenase (ADH) explains various metabolic effects of ethanol but does not account for the tolerance and a number of associated disorders that develop in the alcoholic. These were elucidated by the discovery of the microsomal metabolism of ethanol. The physiologic role of this system comprises gluconeogenesis from ketones, fatty acid metabolism, and detoxification of xenobiotics, including ethanol. After chronic ethanol consumption, the activity of the microsomal ethanol-oxidizing system (MEOS) increases, with an associated rise in cytochromes P-450, especially CYP2E1. This induction is associated with proliferation of the endoplasmic reticulum, both in experimental animals and in humans. The role of MEOS in vivo and its increase after chronic ethanol consumption was shown most conclusively in alcohol dehydrogenase-negative deer mice. Enhanced ethanol oxidation is associated with cross-induction of the metabolism of other drugs, resulting in drug tolerance. Furthermore, there is increased conversion of known hepatotoxic agents (such as **CCl4**) to **toxic** metabolites, which may explain the enhanced susceptibility of alcoholics to the adverse effects of industrial solvents. CYP2E1 also has a high capacity to activate some commonly used drugs, such as acetaminophen, to their **toxic** metabolites, and to promote carcinogenesis (e.g., from dimethylnitrosamine). Moreover, catabolism of retinol is accelerated and there also is induction of microsomal enzymes involved in lipoprotein production, resulting in hyperlipemia. Contrasting with the chronic effects of ethanol consumption, acute ethanol intake inhibits the metabolism of other drugs through competition for the at least partially shared microsomal pathway. In addition, metabolism by CYP2E1 results in a significant free radical release and acetaldehyde production which, in turn, diminish reduced glutathione (GSH) and other defense systems against oxidative stress. Acetaldehyde also formsadducts with proteins, thereby altering the functions of mitochondria and of repair enzymes. Increases of CYP2E1 and its mRNA prevail in the perivenular zone, the area of maximal liver damage. CYP1A2 and CYP3A4, two other perivenular P-450s, can also sustain the metabolism of ethanol, thereby contributing to MEOS activity and possibly liver injury. By contrast, CYP2E1 inhibitors oppose alcohol-induced liver damage, but heretofore available compounds were too **toxic** for clinical use. Recently, however,

polyenylphosphatidylcholine (PPC), an innocuous mixture of polyunsaturated lecithins extracted from soybeans, was discovered to decrease CYP2E1 activity. PPC (and its active component dilinoleoylphosphatidylcholine) also oppose hepatic oxidative stress and fibrosis. PPC is now being tested clinically for the prevention and treatment of liver disease in the alcoholic.

L4 ANSWER 3 OF 85 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:11892 BIOSIS
DN PREV200000011892
TI Attenuated liver fibrosis and depressed serum albumin levels in **carbon tetrachloride**-treated IL-6-deficient mice.
AU Natsume, Miyoko; Tsuji, Hirokazu; Harada, Akihisa; Akiyama, Mariko; Yano, Tomoyuki; Ishikura, Hiroshi; Nakanishi, Isao; Matsushima, Kouji; Kaneko, Shu-ichi; Mukaida, Naofumi [Reprint author]
CS Department of Molecular Oncology, Cancer Research Institute, Kanazawa University, 13-1 Takara-machi, Kanazawa, 920-0934, Japan
SO Journal of Leukocyte Biology, (Oct., 1999) Vol. 66, No. 4, pp. 601-608. print.
CODEN: JLBIE7. ISSN: 0741-5400.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 23 Dec 1999
Last Updated on STN: 31 Dec 2001
AB Chronic intermittent injection of **carbon tetrachloride** (**CCl4**) for more than 10 weeks induced liver fibrosis in mice, as evidenced by positive Azan staining and increased intrahepatic collagen content. Preceding the onset of liver fibrosis, interleukin-6 (IL-6) **gene expression** was enhanced in liver and immunoreactive IL-6 was detected in infiltrating inflammatory cells. To delineate the role of IL-6 in this process, we treated IL-6-deficient mice with **CCl4** in a similar manner for 12 weeks, after which fibrotic changes were less evident and serum albumin levels were lower in IL-6-deficient than wild-type mice. Moreover, **CCl4**-induced expression of transforming growth factor beta1 and hepatocyte growth factor genes in liver was significantly reduced in IL-6-deficient mice. Thus, IL-6 may be vitally involved in fibrotic changes and maintenance of serum albumin levels, partly by modulating intrahepatic expression of these cytokines.

L4 ANSWER 4 OF 85 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:444324 BIOSIS
DN PREV199900444324
TI Analysis of altered hepatocyte **gene expression** induced by **carbon tetrachloride** (**CCl4**) using **microarray** technology.
AU Holden, P. R. [Reprint author]; James, N. H. [Reprint author]; Brooks, A. N. [Reprint author]; Roberts, R. A. [Reprint author]; Kimber, I. [Reprint author]; Pennie, W. D. [Reprint author]
CS Zeneca Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK
SO Human and Experimental Toxicology, (Aug., 1999) Vol. 18, No. 8, pp. 522. print.
Meeting Info.: Annual Congress of the British Toxicology Society. Stoke on Trent, England, UK. April 18-21, 1999. British Toxicology Society.
CODEN: HETOEA. ISSN: 0960-3271.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 26 Oct 1999
Last Updated on STN: 26 Oct 1999

L4 ANSWER 5 OF 85 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:137826 BIOSIS
DN PREV199900137826
TI Acute **carbon tetrachloride** feeding selectively damages large, but not small, cholangiocytes from normal rat liver.
AU Lesage, Gene D.; Benedetti, Antonio; Glaser, Shannon; Marucci, Luca; Tretjak, Ziga; Caligiuri, Alessandra; Rodgers, Rebecca; Phinizy, Jo Lynne; Baiocchi, Leonardo; Francis, Heather; Lasater, John; Ugili, Laura; Alpini, Gianfranco [Reprint author]
CS Intern. Med. Med. Physiol., Texas A and M Univ. Health Sci. Cent., Coll. Med. Central Texas Veterans Health Care System, 1901 South 1st Street, Build. 147, Temple, TX 76504, USA
SO Hepatology, (Feb., 1999) Vol. 29, No. 2, pp. 307-319. print.
CODEN: HPTLD9. ISSN: 0270-9139.
DT Article
LA English
ED Entered STN: 31 Mar 1999
Last Updated on STN: 31 Mar 1999
AB The aim of this study was to develop a model of selective duct damage restricted to hormone-responsive segments corresponding to the ducts damaged in primary biliary cirrhosis (PBC). **Carbon tetrachloride** (**CCl4**) was fed by gavage to rats, and 2, 7, 14, and 28 days later, small and large cholangiocytes were isolated. Apoptosis was determined in situ by morphology and in purified cholangiocytes by assessment of nuclear fragmentation by 4,6-diamidino-2-phenylindole (DAPI) staining. Cholangiocyte proliferation was evaluated in situ by morphometry of liver sections stained for cytokeratin-19 (CK-19) and by proliferating cellular nuclear antigen (PCNA) staining in liver sections and in purified cholangiocytes by PCNA **gene expression**. Ductal secretion was assessed by measurement of secretin receptor (SR) **gene expression** and secretin-induced cyclic adenosine 3',5'-monophosphate (cAMP) synthesis and secretin-induced choleresis. Two days after **CCl4** administration, there was an increased number of small ducts, but a reduction of large ducts. Apoptosis, observed only in large ducts, was associated with decreased DNA synthesis and ductal secretion. Conversely, small cholangiocytes expressed de novo the SR gene and secretin-stimulated cAMP synthesis 2 days after **CCl4** treatment. Proliferation of large cholangiocytes was delayed until 7 days, which was associated with a transient increase in ductal secretion in vivo. **CCl4** effects on cholangiocytes were reversed by day 28.

L4 ANSWER 6 OF 85 MEDLINE on STN
AN 2000021651 MEDLINE
DN PubMed ID: 10552896
TI Two assays for measuring fibrosis: reverse transcriptase-polymerase chain reaction of collagen alpha(1) (III) mRNA is an early predictor of subsequent collagen deposition while a novel serum N-terminal procollagen (III) propeptide assay reflects manifest fibrosis in **carbon tetrachloride**-treated rats.
AU Kauschke S G; Knorr A; Heke M; Kohlmeyer J; Schauer M; Theiss G; Waehler R; Burchardt E R
CS Pharmaceutical Research Center, Bayer AG, Wuppertal, D-42096, Germany.
SO Analytical biochemistry, **(1999 Nov 15)** 275 (2) 131-40.
Journal code: 0370535. ISSN: 0003-2697.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 20000113

Last Updated on STN: 20000113
Entered Medline: 19991214

AB Using a novel quantitative reverse transcriptase-polymerase chain reaction assay, we have determined the amount of specific mRNA for procollagen alpha(1) (III) (PIIIP) in the **carbon tetrachloride** (CCl(4)) model of liver fibrosis in rats. After a single week of CCl(4) application, the amount of PIIIP mRNA was increased approximately 10 times over the untreated control group and continued to increase to approximately 30 times after 7 weeks of intoxication. In this model substantial fibrosis was demonstrated by computer-aided morphometry after 5 to 7 weeks of treatment. Using recombinant murine N-terminal procollagen alpha(1) (III) propeptide (PIIINP), a novel sensitive immunoassay for the measurement of circulating PIIINP in rodent sera was established. An increase in PIIINP serum levels was observed after 5 to 7 weeks of CCl(4) intoxication. Our results suggest PIIIP **gene expression** is an early marker of tissue fibrosis. Early PIIIP **gene expression** is correlated with the extent of the subsequent fibrosis. PIIIP mRNA levels increase much earlier than conventional histological examination or PIIINP levels. PIIINP measurements with our new serum assay, on the other hand, are a good noninvasive marker of manifest fibrosis but are a poor marker of fibrogenesis.
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L4 ANSWER 7 OF 85 MEDLINE on STN
AN 1999439699 MEDLINE
DN PubMed ID: 10508906
TI Hepatoprotective action of adenovirus-transferred HNF-3gamma gene in acute liver injury caused by CCl(4).
AU Nakamura T; Akiyoshi H; Shiota G; Isono M; Nakamura K; Moriyama M; Sato K
CS Department of Molecular Biology, Faculty of Medicine, Tottori University, Yonago, Japan.
SO FEBS letters, **(1999 Oct 1)** 459 (1) 1-4.
Journal code: 0155157. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199911
ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991101

AB Hepatocyte nuclear factor-3gamma (HNF-3gamma) is an important regulator of liver-specific genes and the expression of this factor is reduced in the liver injured by **carbon tetrachloride** (CCl(4)).
Wistar rats were infected with a recombinant adenovirus carrying the cDNA for HNF-3gamma (AxCAHNF3gamma) via the tail vein and were treated with CCl(4) by intraperitoneal injection. Liver damage, such as swelling of the hepatocytes and increases in serum marker enzymes were markedly alleviated by AxCAHNF3gamma infection. Interestingly, hepatocyte growth factor (HGF) was strongly induced in the AxCAHNF3gamma-infected liver. Likewise, HNF-1alpha and HNF-1beta levels were increased, but HNF-3alpha and HNF-3beta levels were depressed in the liver. Our results suggest that the transduced HNF-3gamma gene leads to a hepatoprotective effect via the induction of HGF by the combined actions of liver-enriched transcription factors.

L4 ANSWER 8 OF 85 MEDLINE on STN
AN 1998196790 MEDLINE
DN PubMed ID: 9537443
TI Hepatic oval cell activation in response to injury following chemically induced periportal or pericentral damage in rats.

AU Petersen B E; Zajac V F; Michalopoulos G K
CS Department of Pathology, University of Pittsburgh, PA 15261, USA.
NC CA30241 (NCI)
CA35373 (NCI)
SO Hepatology (Baltimore, Md.), **(1998 Apr)** 27 (4) 1030-8.
Journal code: 8302946. ISSN: 0270-9139.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980416
AB Administration of 2-acetylaminofluorene (2-AAF) given before partial hepatectomy (PHx) results in suppression of hepatocyte proliferation and stimulation of oval cell proliferation. Our objective in this study was to examine the oval cell response and associated alpha-fetoprotein (AFP) **gene expression** by combining 2-AAF with selective damage of centrilobular regions (**carbon tetrachloride** [**CCl4**]) or periportal regions (allyl alcohol [AA]). Centrilobular damage results in a more enhanced oval cell response and AFP **gene expression** than periportal damage. Conversely, more intense proliferation of intraportal bile duct epithelia was seen with 2-AAF/AA than with 2-AAF/**CCl4**. The oval cell response and AFP **gene expression** was ranked as 2-AAF/ **CCl4** > or = 2-AAF/PHx > 2-AAF/AA. AFP mRNA expression was also examined in an acute AA and **CCl4** injury. We found very little AFP **gene expression** compared with the 2-AAF/hepatic injury models. To see a true oval cell response, the hepatocytes must be inhibited from proliferating. In addition, the results presented with the 2-AA/AA model suggest that the periportal matrix may be as important as the cells that populate the area.

L4 ANSWER 9 OF 85 MEDLINE on STN
AN 1998196787 MEDLINE
DN PubMed ID: 9537440
TI (Latent) transforming growth factor beta in liver parenchymal cells, its injury-dependent release, and paracrine effects on rat hepatic stellate cells.
AU Roth S; Michel K; Gressner A M
CS Department of Clinical Chemistry, Philipps University, Marburg, Germany.
SO Hepatology (Baltimore, Md.), **(1998 Apr)** 27 (4) 1003-12.
Journal code: 8302946. ISSN: 0270-9139.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980422
Last Updated on STN: 19980422
Entered Medline: 19980416
AB Cultured parenchymal liver cells (PC) were recently recognized to contain (latent) transforming growth factor beta (TGF-beta) while the expression of TGF-beta mRNA remains controversial. This study was designed to analyze PC in different microenvironments (liver in situ, highly purified, isolated, and cultured PC) regarding the qualitative and quantitative content of mature and latent TGF-beta protein (immunostainings, enzyme-linked immunosorbent assay [ELISA], and enzyme-labeled fluorescence [ELF] technique). The results were compared with its **gene expression** (reverse-transcription polymerase chain reaction [RT-PCR]). In all microenvironments, PC contained latent TGF-beta, which

was partially activated after cell isolation and culture. The amount of total TGF-beta (mature plus latent) of latency-associated peptide (LAP) and of latent TGF-beta binding protein (LTBP) were shown to decrease during culture. In contrast, TGF-beta2 and TGF-beta3 mRNA and LTBP-1 and -3 mRNA expression were first detectable after culture. Permeabilization of cell membranes in whole liver and of isolated PC with streptolysin O or **carbon tetrachloride**, respectively, released TGF-beta, a part of which was integrated in the large latent complex as estimated by analytical gel filtration chromatography. The TGF-beta released by damaged PC induces paracrine effects on hepatic stellate cell cultures. It stimulates hyaluronan synthesis and antagonizes the effect of mitogenic factor(s) of PC on [3H]thymidine incorporation. The results strongly suggest that the main part of hepatocellular TGF-beta is not generated by de novo synthesis but from uptake into the liver in vivo. The immunodetection of preexisting mature TGF-beta after isolation of the cells is probably caused by intracellular activation of latent TGF-beta. The injury-dependent discharge of TGF-beta from PC might be an important mechanism for initiation and perpetuation of various forms of chronic human liver diseases.

L4 ANSWER 10 OF 85 MEDLINE on STN
AN 1998358189 MEDLINE
DN PubMed ID: 9691091
TI Mechanisms of spontaneous resolution of rat liver fibrosis. Hepatic stellate cell apoptosis and reduced hepatic expression of metalloproteinase inhibitors.
AU Iredale J P; Benyon R C; Pickering J; McCullen M; Northrop M; Pawley S; Hovell C; Arthur M J
CS University Medicine, University of Southampton, Hampshire SO16 6YD, United Kingdom.
SO Journal of clinical investigation, **(1998 Aug 1)** 102 (3) 538-49.
Journal code: 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199808
ED Entered STN: 19980903
Last Updated on STN: 20000303
Entered Medline: 19980826
AB Liver fibrosis results from the excessive secretion of matrix proteins by hepatic stellate cells (HSC), which proliferate during fibrotic liver injury. We have studied a model of spontaneous recovery from liver fibrosis to determine the biological mechanisms mediating resolution. Livers were harvested from rats at 0, 3, 7, and 28 d of spontaneous recovery from liver fibrosis induced by 4 wk of twice weekly intraperitoneal injections with **CCl4**. Hydroxyproline analysis and histology of liver sections indicated that the advanced septal fibrosis observed at time 0 (peak fibrosis) was remodeled over 28 d of recovery to levels close to control (untreated liver). alpha-Smooth muscle actin staining of liver sections demonstrated a 12-fold reduction in the number of activated HSC over the same time period with evidence of HSC apoptosis. Ribonuclease protection analysis of liver RNA extracted at each recovery time point demonstrated a rapid decrease in expression of the collagenase inhibitors TIMP-1 and TIMP-2, whereas collagenase mRNA expression remained at levels comparable to peak fibrosis. Collagenase activity in liver homogenates increased through recovery. We suggest that apoptosis of activated HSC may vitally contribute to resolution of fibrosis by acting as a mechanism for removing the cell population responsible for both producing fibrotic neomatrix and protecting this matrix from degradation via their production of TIMPs.

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L4 ANSWER 11 OF 85 MEDLINE on STN DUPLICATE 1
AN 1998234092 MEDLINE
DN PubMed ID: 9574820
TI Partial hepatoprotective effects of allylthiobenzimidazole in the absence of cytochrome P4502E1 suppression: effects on epoxide hydrolase, rGSTA2, rGSTA3/5, rGSTM1 and rGSTM2 expression.
AU Kim S G; Lee A K; Kim N D
CS College of Pharmacy, Duksung Women's University, Seoul, Korea.
SO Xenobiotica; fate of foreign compounds in biological systems, **(1998 Mar)** 28 (3) 323-36.
Journal code: 1306665. ISSN: 0049-8254.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980618
Last Updated on STN: 19980618
Entered Medline: 19980611
AB 1. 2-(Allylthio)pyrazine protects the liver against acetaminophen- and **carbon tetrachloride**-induced injury through inhibition of cytochrome P4502E1 and induction of glutathione S-transferases (GSTs). By comparison, the effects of allylthiobenzimidazole (ATB) on the levels of several hepatic cytochrome P450, microsomal epoxide hydrolase (mEH) and GST expression have been studied in the rat herein. 2. Western immunoblotting analyses revealed that ATB treatment (50 mg/kg/day for 5 days) failed to alter cytochrome P4501A2, P4502B1/2 and P4502E1 levels in the liver, whereas the expression of P4502C11 was reduced approximately 50% by ATB. 3. Treatment of rat with a single dose of ATB resulted in 2-21-fold increases in mEH mRNA levels at 24 h with an ED50 = 60 mg/kg. mEH mRNA level was elevated 9- and 21-fold at 12 and 24 h after treatment at 200 mg/kg respectively as compared with control. Western blot analysis revealed that ATB induced mEH protein levels by 2-fold relative to control. 4. ATB induced the major GST mRNA levels as a function of dose, resulting in rGSTA2, rGSTA3/5 and rGSTM1 mRNA levels elevated by 20-, 6- and 8-fold at 24 h respectively. The relative rGSTM2 mRNA level was minimally affected. Time-course studies showed that mEH, rGSTA2 and rGSTM1 mRNA levels were significantly increased at 12 and 24 h after ATB treatment, returning to control levels by 48 h. Treatment of rat with ATB (20-50 mg/kg/day for 5 days) resulted in 2-3-fold increases in mEH, rGSTA1/2, rGSTA3/5 and rGSTM1 mRNA levels with the induction of GST subunits. 5. ATB failed to block **carbon tetrachloride**-induced liver **toxicity** in rat and mouse. ATB treatment (50 mg/kg day for 3 days) prior to a lethal dose of acetaminophen significantly reduced acetaminophen-induced liver **toxicity** in mouse, as assessed by both plasma alanine aminotransferase activity and histopathological examination. The 30-day survival rate of mouse gamma-irradiated at 8 Gy failed to be improved by ATB pretreatment (100 mg/kg/day for 2 days). 6. These results provided evidence that ATB stimulated mEH and GST **gene expression** at early times and reduced the P4502C11 level in the absence of P4502E1 suppression. ATB was only partially effective in protecting the liver against **toxicant**-induced injury despite the presence of allylthio moiety in its chemical structure.

L4 ANSWER 12 OF 85 MEDLINE on STN
AN 1998042120 MEDLINE
DN PubMed ID: 9374707
TI Pentoxifylline blocks hepatic stellate cell activation independently of

phosphodiesterase inhibitory activity.
AU Lee K S; Cottam H B; Houglum K; Wasson D B; Carson D; Chojkier M
CS Department of Medicine, Veterans Affairs Medical Center, San Diego, California, USA.
NC DK-38652 (NIDDK)
DK-46971 (NIDDK)
GM-23200 (NIGMS)
+
SO American journal of physiology, **(1997 Nov)** 273 (5 Pt 1) G1094-100.
Journal code: 0370511. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 20000303
Entered Medline: 19971217
AB Activated, but not quiescent, hepatic stellate cells (lipocytes) have a high level of collagen type I and smooth muscle actin (SMA) **gene expression**. Therefore, stellate cell activation is a critical step in hepatic fibrosis. The mechanisms leading to stellate cell activation in vivo are unknown. The characteristic hepatic oxidative stress cascade induced in rats by **CCl4** markedly stimulated stellate cell entry into S phase, nuclear factor (NF)-kappa B activity, and c-myb expression. These changes were prevented by pentoxifylline, which also decreased **CCl4**-induced hepatic injury. As expected, cAMP-mediated phosphorylation of CREB-Ser133 was induced in vivo in stellate cells by pentoxifylline but not by its metabolite 5, an N-1 carboxypropyl derivative, which lacks phosphodiesterase inhibitory activity. Stellate cell nuclear extracts from **CCl4**-treated, but not from control, animals formed a complex with the critical promoter E box of the alpha-SMA gene, which was disrupted by c-myb antibodies and competed with by c-myb cognate DNA. Treatment with pentoxifylline or metabolite 5 prevented the molecular abnormalities characteristic of stellate cell activation induced by **CCl4**. These results suggest that induction of c-myb plays an important role in the in vivo activation of stellate cells. Pentoxifylline blocks stellate cell activation in vivo independently of its inhibitory effects on phosphodiesterases by interfering with the oxidative stress cascade and the activation of NF-kappa B and c-myb.

L4 ANSWER 13 OF 85 MEDLINE on STN DUPLICATE 2
AN 97445293 MEDLINE
DN PubMed ID: 9300178
TI p53-independent induction of p21WAF1/CIP1 expression in pericentral hepatocytes following **carbon tetrachloride** intoxication.
AU Serfas M S; Goufman E; Feuerman M H; Gartel A L; Tyner A L
CS Department of Genetics, University of Illinois at Chicago 60607, USA.
NC CA55739 (NCI)
DK48836 (NIDDK)
SO Cell growth & differentiation : molecular biology journal of the American Association for Cancer Research, **(1997 Sep)** 8 (9) 951-61.
Journal code: 9100024. ISSN: 1044-9523.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971105

Last Updated on STN: 19971105
Entered Medline: 19971021

AB The cyclin-dependent kinase, proliferating cell nuclear antigen, and stress-activated protein kinase/c-jun NH2 terminal kinase inhibitor p21WAF1/CIP1 can induce G1 arrest, and its expression coincides with the cessation of replication in many systems. We examined expression of p21 during the early stages of **carbon tetrachloride** intoxication in the mouse liver and observed a dramatic increase in p21 RNA levels between 4 and 8 h after administration. p21 expression, visualized by in situ hybridization, is induced in pericentral hepatocytes before **carbon tetrachloride**-induced necrosis. Examination of c-fos and c-myc expression patterns confirm that these immediate-early genes are induced in similar regions of the mouse liver. p21 induction is not dependent on p53; we observed similar levels and localization of p21 in wild-type and p53 null animals. Immunohistochemical localization of p21 and CCAAT/enhancer-binding protein expression shows that p21 protein accumulation is limited to a subset of CCAAT/enhancer-binding protein-positive hepatocytes. A second peak of periportal and intermediate zone-specific p21 **gene expression**, appearing 1-2 days after injection, is also p53 independent and may represent cell cycle checkpoints or postmitotic growth arrest. Sporadic p21 expression was also detected in pairs of hepatocytes distributed throughout the liver acini in healthy animals. Together, these data suggest several roles for p21 in the liver in response to **toxicity**, regeneration, and growth inhibition.

L4 ANSWER 14 OF 85 MEDLINE on STN
AN 97468657 MEDLINE
DN PubMed ID: 9327722
TI Bile ductular damage induced by methylene dianiline inhibits oval cell activation.
AU Petersen B E; Zajac V F; Michalopoulos G K
CS Department of Pathology, University of Pittsburgh, Pennsylvania 15261, USA.
NC CA30241 (NCI)
CA35373 (NCI)
SO American journal of pathology, **(1997 Oct)** 151 (4) 905-9.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199710
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971030

AB Administration of 2-acetylaminofluorene (2-AAF) given before a two-thirds partial hepatectomy (PHx), results in suppression of hepatocyte proliferation and stimulation of oval cell proliferation. Our objective in this study was to examine the oval cell response and associated alpha-fetoprotein (AFP) **gene expression** by combining 2-AAF with selective hepatic damage caused by either **carbon tetrachloride** (**CCl4**) exposure or by PHx. We also examined oval cell response with the above two protocols (2-AAF/**CCl4** and 2-AAF/PHx) as affected by previous bile ductular damage caused by 4,4'-methylene dianiline (4,4'-diaminodiphenylmethane, DAPM) exposure. DAPM is an aromatic diamine, known to cause bile ductular damage in both humans and animals. Using the protocols of 2-AAF/**CCl4** and 2-AAF/PHx, when DAPM was given 24 hours before the hepatic injury, no oval cell proliferation was seen (histological) and AFP expression was not detected by Northern blot analysis. These results provide direct evidence that oval cells are closely associated with the

biliary epithelial cells and supports the theory that hepatic oval cells may originate from cells derived from either intraportal or periportal ductules.

L4 ANSWER 15 OF 85 MEDLINE on STN
AN 97201417 MEDLINE
DN PubMed ID: 9049203
TI Liver cell proliferation induced by nafenopin and cyproterone acetate is not associated with increases in activation of transcription factors NF-kappaB and AP-1 or with expression of tumor necrosis factor alpha.
AU Menegazzi M; Carcereri-De Prati A; Suzuki H; Shinozuka H; Pibiri M; Piga R; Columbano A; Ledda-Columbano G M
CS Dipartimento di Biochimica, Universita di Verona, Italy.
NC CA53453 (NCI)
SO Hepatology (Baltimore, Md.), **(1997 Mar)** 25 (3) 585-92.
Journal code: 8302946. ISSN: 0270-9139.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970320
AB Our previous studies have shown a different pattern of immediate early gene and growth factor **gene expression** between compensatory liver regeneration occurring after cell loss/death and direct hyperplasia induced by primary mitogens. In the present study, modifications in the activation of two transcription factors, NF-kappaB and AP-1; steady-state levels of tumor necrosis factor alpha (TNF-alpha) messenger RNA (mRNA); and induction of the inducible nitric oxide synthase (iNOS) were examined in rat liver during different types of cell proliferation. Compensatory regeneration was induced in male Wistar rats by partial hepatectomy of two thirds (PH) or a necrogenic dose of **CCl4** (2 mL/kg), whereas direct hyperplasia was induced by a single administration of the primary mitogens lead nitrate (LN, 100 micromol/kg), cyproterone acetate (CPA, 60 mg/kg), or nafenopin (NAF, 200 mg/kg). Liver regeneration after treatment with **CCl4** was associated with an increase in steady-state levels of TNF-alpha mRNA, activation of NF-kappaB and AP-1, and induction of iNOS. A strong and prolonged activation of NF-kappaB but not of AP-1 was observed in LN-induced hyperplasia. LN also induced an increase in hepatic levels of TNF-alpha and iNOS mRNA. On the other hand, direct hyperplasia induced by two other primary mitogens, NAF and CPA, occurred in the complete absence of modifications in the hepatic levels of TNF-alpha mRNA, activation of NF-kappaB and AP-1, or induction of iNOS, although the number of hepatocytes entering S phase 18 to 24 hours after NAF was similar to that seen after PH. These results add further support to the hypothesis that cell proliferation occurring in the absence of cell loss/death may be triggered by unknown signaling pathways different from those responsible for the transition of hepatocytes from G0 to G1 after PH or cell necrosis.

L4 ANSWER 16 OF 85 MEDLINE on STN
AN 97381180 MEDLINE
DN PubMed ID: 9238536
TI Role of H-ras gene in chronic liver damage in mice. By using transgenic mice carrying a human C-H-ras proto-oncogene without mutations.
AU Tsunematsu S; Saito H; Sato R; Morizane T; Ishii H
CS Department of Medicine, Kanagawa Dental College, Japan.
SO Biochemistry and molecular biology international, **(1997 Jun)** 42 (2) 371-9.
Journal code: 9306673. ISSN: 1039-9712.

CY Australia
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971024
Last Updated on STN: 20000303
Entered Medline: 19971014
AB Hepatic tumors including hepatocellular carcinoma were generated by **carbon tetrachloride** in transgenic mice carrying a human c-H-ras gene (rasH2 mice). RasH2 mice express 2 to 3 times more ras protein (ras p21) in the liver than do non-Tg mice. When **carbon tetrachloride** was administered, the rasH2 mice produced about 5 times as many hepatic tumors than did the non-transgenic mice. However, neither the 10-100 times higher ras p21 expression required for murine fibroblast transformation by itself nor the mutational activation of the H-ras gene was observed in **carbon tetrachloride** -induced hepatic tumors. These results show that H-ras proto-oncogene expression in the murine liver, even if it is not high enough to transform cells, also causes liver tumors when CC1(4) are repeatedly given.

L4 ANSWER 17 OF 85 MEDLINE on STN
AN 97212698 MEDLINE
DN PubMed ID: 9059516
TI Viscosity regulates apolipoprotein A-1 **gene expression** in experimental models of secondary hyperlipidemia and in cultured hepatocytes.
AU Nuno P; Hernandez A; Mendoza-Figueroa T; Panduro A
CS Institute of Molecular Biology in Medicine, C.U.C.S. Universidad de Guadalajara, Jalisco, Mexico.
SO Biochimica et biophysica acta, **(1997 Feb 18)** 1344 (3) 262-9.
Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970407
Last Updated on STN: 19970407
Entered Medline: 19970326
AB This study analyzes the relationship of plasmatic colloid osmotic pressure (PCO) and viscosity with the different hyperlipidemic stages observed in rats with acute liver damage induced by **carbon tetrachloride** (**CCl4**) and in rats with nephrotic syndrome induced by puromycin amino nucleoside (PAN). In both animal models viscosity increases were associated with the induction of the hyperlipidemic stage characterized by an increase of high density lipoproteins (HDL) and steady-state levels (SSL) of apo A-1 mRNA. In both animal models PCO decreased at early stages of the disease when hyperlipidemia was characterized principally by an increase of total cholesterol and triacylglycerols, but was not associated with the induction of HDL and apo A-1 mRNA. To confirm the in vivo findings, we studied the effect of viscosity on apo A-1 **gene expression** in an in vitro model using cultured hepatocytes. When medium viscosity was maintained below physiological values, an induction of the SSL of apo A-1 mRNA was observed. By contrast, when medium viscosity was raised to values similar or higher than the physiological range, the SSL of apo A-1 mRNA decreased steadily and after 24 h incubation an almost total inhibition was observed. These results suggest that in both experimental animal models of secondary hyperlipidemia, small viscosity changes below the physiological range, most probably in the interstitial fluid, can induce apo A-1 **gene expression**

at the mRNA level, and that when viscosity reaches physiological values, apo A-1 **gene expression** is inhibited. Both effects were shown in cultured hepatocytes.

L4 ANSWER 18 OF 85 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:514415 BIOSIS
DN PREV199799813618
TI Antisense S-oligodeoxynucleotides down-regulate TGF-beta-production by Kupffer cells from CCl-4-injured rat livers.
AU Armendariz-Borunda, Juan [Reprint author]; Legros., Leighton, Jr.; Campollo, Octavio; Panduro, Arturo; Rincon, Ana Rosa
CS Inst. Molecular Biol. Med., CUCS, Univ. Guadalajara, Apdo. Postal 2-500, Guadalajara, Jal 44281, Mexico
SO Biochimica et Biophysica Acta, (1997) Vol. 1353, No. 3, pp. 241-252. CODEN: BBACAQ. ISSN: 0006-3002.
DT Article
LA English
ED Entered STN: 10 Dec 1997
Last Updated on STN: 10 Dec 1997
AB TGF-beta is a pleiotropic cytokine involved in multiple physiological and pathophysiological regulatory mechanisms. Since TGF-beta is a disparate modulator of cell recruitment, proliferation and extracellular matrix phenotype for mesenchymal and nonmesenchymal cells, we have been investigating the role of this cytokine in the pathophysiology of liver. In the present paper we investigate which hepatic cell types from CCl-4-injured rat livers express TGF-beta mRNA and produce TGF-beta in culture, with the aim of further obliterating its biological activity by means of antisense technology. We performed a series of comprehensive molecular studies of in situ hybridization, northern blots, and RT-PCR and we found that only non-parenchymal cells produce TGF-beta while its expression in hepatocytes was absent. Consistent with the in situ hybridization findings, we observed that Kupffer cells expressed high steady-state levels of TGF-beta mRNA, while circulating monocytes expressed a smaller amount of TGF-beta transcripts. We did not detect TGF-beta **gene expression** in endothelial cells. These findings were further confirmed by RT-PCR analyses. TGF-beta activity, as measured by inhibition of (3H)thymidine incorporation by Mv 1 Lu mink lung epithelial cells, was down-regulated in culture by antisense phosphorothioate oligonucleotides. These effects of antisense oligomers were dose-dependent and the sense oligonucleotides had no effect at the same concentration.

L4 ANSWER 19 OF 85 MEDLINE on STN
AN 97443696 MEDLINE
DN PubMed ID: 9298488
TI **Gene expression** in liver after **toxic** injury: analysis of heat shock response and oxidative stress-inducible genes.
AU Schiaffonati L; Tiberio L
CS Dipartimento di Scienze Biomediche e Biotecnologie, Universita degli Studi di Brescia, Italy.
SO Liver, **(1997 Aug)** 17 (4) 183-91. Journal code: 8200939. ISSN: 0106-9543.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971105
Last Updated on STN: 19980206
Entered Medline: 19971023
AB In the liver, **CCl4** induces cell necrosis followed by regeneration. Cell injury is caused by free radical damage and may be

due, at least in part, to oxidative stress and the subsequent formation of reactive oxygen intermediates (ROIs). In a rat model of acute **CCl4**-induced hepatic injury, we examined the expression of genes involved in cellular response to different kinds of stress, including oxidative stress (hsp 70 family, heme oxygenase), in free radical detoxification (Mn superoxide dismutase and Cu/ Zn superoxide dismutase), in iron homeostasis (H and L ferritin subunits) and in the cell cycle (c-fos, c-jun, histone H3). As an experimental approach, we first analysed the pattern of protein synthesised by liver slices in vitro. Then we studied the mechanisms regulating the expression of different genes, by analysing both mRNA steady state levels and transcription rates. Activation of the specific heat shock transcription factor (HSF) by **CCl4** was also investigated. We observed that different members of the hsp70 family (hsp70, hsc73, grp78) are activated by different kinetics and are regulated mainly at the transcriptional level. Induction of the hsp70 gene occurs rapidly and transiently and is preceded by the activation of HSF DNA-binding activity. We demonstrated an increase in the steady-state levels of mRNAs for heme oxygenase, Mn and Cu/Zn superoxide dismutases and H and L ferritin subunits. However, different kinetics and regulatory mechanisms occurred with different genes. We showed that induction of c-fos and c-jun protooncogenes is the earliest event after **CCl4** administration, whereas histone H3 expression peaked at 24-48 h. The results of this study are interpreted as evidence that activation of specific stress response genes is primarily related to the defence against the rapidly occurring cell damage, but may also be related to subsequent processes of tissue inflammation and cell proliferation.

L4 ANSWER 20 OF 85 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:408390 BIOSIS
DN PREV199799714593
TI The effect of aflatoxin B1 on the expression of early response genes and transforming growth factor-alpha in CCl-4 induced rat liver injury.
AU Hong, Soon Won [Reprint author]; Park, Chanil
CS Dep. Pathol., Yonsei Univ., Wonju Coll. Med., Ilsan-Dong 162, Wonju, Kangwon-Do, South Korea
SO Yonsei Medical Journal, (1997) Vol. 38, No. 3, pp. 167-177.
CODEN: YOMJA9. ISSN: 0513-5796.
DT Article
LA English
ED Entered STN: 24 Sep 1997
Last Updated on STN: 24 Sep 1997
AB Aflatoxin B1(AFB1), a fungal toxin produced by Aspergillus flavus, is known to be a possible hepatocarcinogen. But the molecular biologic changes which may occur following exposure to AFB1 are not known and thus the carcinogenesis is not vet understood. This study was performed to examine the expressions of c-myc, c-fos and TGF-alpha genes and to investigate the possible role of those molecular biologic changes in hepatic regeneration and in the development of hepatocellular carcinoma (HCC). Sprague-Dawley rats were divided into 3 groups: **Carbon tetrachloride** (CCl-4) only was administered to group 1, AFB1 only was administered to group II and a combination of AFB1 and CCl-4 was administered to group III. The animals were sacrificed at 0.5, 1, 2, 6, 12, 24, 48, and 72 hours after treatment. In addition to the examination of the hematoxylin-eosin stained sections, hepatic regeneration and apoptosis were analyzed quantitatively by bromodeoxyuridine (BrdU)-anti-BrdU immunohistochemistry and TUNEL assay utilizing apoptosis kit, respectively. The hepatic expressions of c-myc, c-fos and transforming growth factor-alpha (TGF-alpha) were examined by immunohistochemistry and studied by Western blot. The number of BrdU labelled cells and the degree of necrosis/apoptosis were comparable among the different groups. Livers of the group II rats showed nearly normal

histology without regeneration and necrosis/apoptosis. In groups I and III, the number of BrdU- labelled cells showed an increase at 48 hours after treatment, and the increment was significantly higher in group I than in group III. Most BrdU-labelled cells were mature hepatocytes in group I, whereas in group III they appeared to be less mature. In group I, apoptosis showed an increase at around 24 hours, but appeared in group III as early as 12 hours after treatment and persisted through 48 hours. The expressions of c-myc and c-fos were also different between the experimental groups. The expression intensity of c-myc in group I was highest at 1 hour and decreased thereafter. In groups II and III, the expressions were much more intense than in group I, except at 1 hour, and the increased intensity persisted throughout the experiment. Group II in particular showed a peak intensify at 30 minutes and at 6 hours after treatment. In group I, c-fos was strongly expressed only at 24 hours, but in group III, there was progressively increased expression with peak intensity at 24 hours. TGF-alpha was expressed in similar intensities in all groups throughout the experiment. These results suggest that AFB1 may evoke an intense and protracted expression of c-myc, provocating the CCl-4-induced necrosis of hepatocytes, and a prolonged expression of c-fos, inducing persistent signals for regeneration which in turn may activate the replication of immature cells. These findings will aid further investigation of molecular biologic and histologic characteristics of the hepatotoxic and hepatocarcinogenic mechanism of AFB1 in rats. And these results in rats, together with clinico-epidemiologic and molecular biologic investigations in humans and other animals, suggest that AFB1 may supply hepatocarcinogenic background in early exposure time in AFB1-contaminated areas of China and Korea.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	21.81	22.02

STN INTERNATIONAL LOGOFF AT 18:11:56 ON 19 MAR 2004

result in loss of user privileges and other penalties.

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FILE 'HOME' ENTERED AT 12:43:58 ON 19 MAR 2004

=> s expression and principal component
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> file .pub
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.05	1.05

FILE 'MEDLINE' ENTERED AT 12:47:08 ON 19 MAR 2004

FILE 'BIOSIS' ENTERED AT 12:47:08 ON 19 MAR 2004
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=> s expression and principal component
L1 687 EXPRESSION AND PRINCIPAL COMPONENT

=> s gene expression and principal component
L2 283 GENE EXPRESSION AND PRINCIPAL COMPONENT

=> s l2 and py<2001
L3 69 L2 AND PY<2001

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 51 DUPLICATE REMOVE L3 (18 DUPLICATES REMOVED)

=> d 1-10 bib ab

L4 ANSWER 1 OF 51 MEDLINE on STN
AN 2000396603 MEDLINE
DN PubMed ID: 10748172
TI Caveolin-1 inhibits epidermal growth factor-stimulated lamellipod extension and cell migration in metastatic mammary adenocarcinoma cells (MTLn3). Transformation suppressor effects of adenovirus-mediated gene delivery of caveolin-1.
AU Zhang W; Razani B; Altschuler Y; Bouzahzah B; Mostov K E; Pestell R G; Lisanti M P
CS Department of Molecular Pharmacology, Albert Einstein Cancer Center, Albert Einstein College of Medicine, Bronx, New York 10461, USA.
NC CA-09060 (NCI)
P50-HL56399 (NHLBI)
T32-GM-07288 (NIGMS)
+
SO Journal of biological chemistry, **(2000 Jul 7)** 275 (27) 20717-25.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008

ED Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000816

AB Caveolin-1 is a **principal component** of caveolae membranes that may function as a transformation suppressor. For example, the human caveolin-1 gene is localized to a suspected tumor suppressor locus (D7S522; 7q31.1) that is deleted in human cancers, including mammary carcinomas. However, little is known about the role of caveolins in regulating cell movement, a critical parameter in determining metastatic potential. Here, we examine the role of caveolin-1 in cell movement. For this purpose, we employed an established cellular model, MTLn3, a metastatic rat mammary adenocarcinoma cell line. In this system, epidermal growth factor (EGF) stimulation induces rapid lamellipod extension and cell migration. Interestingly, we find that MTLn3 cells fail to express detectable levels of endogenous caveolin-1. To restore caveolin-1 expression in MTLn3 cells efficiently, we employed an inducible adenoviral gene delivery system to achieve tightly controlled expression of caveolin-1. We show here that caveolin-1 expression in MTLn3 cells inhibits EGF-stimulated lamellipod extension and cell migration and blocks their anchorage-independent growth. Under these conditions, EGF-induced activation of the p42/44 mitogen-activated protein kinase cascade is also blunted. Our results suggest that caveolin-1 expression in motile MTLn3 cells induces a non-motile phenotype.

L4 ANSWER 2 OF 51 MEDLINE on STN DUPLICATE 1
AN 2000437106 MEDLINE
DN PubMed ID: 10940043
TI Developmental control of stress stimulons in Streptomyces coelicolor revealed by statistical analyses of global **gene expression** patterns.
AU Vohradsky J; Li X M; Dale G; Folcher M; Nguyen L; Viollier P H; Thompson C J
CS Biozentrum, University of Basel, CH-4056 Basel, Switzerland.. Charles-J.Thompson@uni-bas.ch
SO Journal of bacteriology, **(2000 Sep)** 182 (17) 4979-86.
Journal code: 2985120R. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921

AB Stress-induced regulatory networks coordinated with a procaryotic developmental program were revealed by two-dimensional gel analyses of global **gene expression**. Four developmental stages were identified by their distinctive protein synthesis patterns using **principal component** analysis. Statistical analyses focused on five stress stimulons (induced by heat, cold, salt, ethanol, or antibiotic shock) and their synthesis during development. Unlike other bacteria, for which various stresses induce expression of similar sets of protein spots, in Streptomyces coelicolor heat, salt, and ethanol stimulons were composed of independent sets of proteins. This suggested independent control by different physiological stress signals and their corresponding regulatory systems. These stress proteins were also under developmental control. Cluster analysis of stress protein synthesis profiles identified 10 different developmental patterns or "synexpression groups." Proteins induced by cold, heat, or salt shock were enriched in three developmental synexpression groups. In addition, certain proteins belonging to the heat and salt shock stimulons were coregulated during development. Thus, stress regulatory systems controlling these stimulons

were implicated as integral parts of the developmental program. This correlation suggested that thermal shock and salt shock stress response regulatory systems either allow the cell to adapt to stresses associated with development or directly control the developmental program.

L4 ANSWER 3 OF 51 MEDLINE on STN DUPLICATE 2
AN 2001190717 MEDLINE
DN PubMed ID: 11126130
TI Computational methods for **gene expression**-based tumor classification.
AU Xiong M; Jin L; Li W; Boerwinkle E
CS University of Texas-Houston Health Science Center, Houston, TX, USA.. mxiong@utsph.sph.uth.tmc.edu
NC GM56515 (NIGMS)
MH59518 (NIMH)
SO BioTechniques, **(2000 Dec)** 29 (6) 1264-8, 1270.
Journal code: 8306785. ISSN: 0736-6205.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405
AB **Gene expression** profiles may offer more or additional information than classic morphologic- and histologic-based tumor classification systems. Because the number of tissue samples examined is usually much smaller than the number of genes examined, efficient data reduction and analysis methods are critical. In this report, we propose a **principal component** and discriminant analysis method of tumor classification using **gene expression** profile data. Expression of 2000 genes in 40 tumor and 22 normal colon tissue samples is used to examine the feasibility of **gene expression**-based tumor classification systems. Using this method, the percentage of correctly classified normal and tumor tissue was 87.0%. The combined approach using **principal components** and discriminant analysis provided superior sensitivity and specificity compared to an approach using simple differences in the expression levels of individual genes.

L4 ANSWER 4 OF 51 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:102626 BIOSIS
DN PREV200100102626
TI Non random chloroplast DNA hypervariability in Medicago sativa.
AU Skinner, D. Z. [Reprint author]
CS USDA-ARS and Agronomy Department, Kansas State University, Throckmorton Hall, Manhattan, KS, 66506-5501, USA
dzolek@ksu.edu
SO Theoretical and Applied Genetics, (December, 2000) Vol. 101, No. 8, pp. 1242-1249. print.
CODEN: THAGA6. ISSN: 0040-5752.
DT Article
LA English
OS Genbank-AF237706; Genbank-AF237707
ED Entered STN: 28 Feb 2001
Last Updated on STN: 15 Feb 2002
AB Two hypervariable regions of the alfalfa (Medicago sativa L) chloroplast genome were used to describe levels of genetic relatedness among populations. PCR primers were developed to amplify the hypervariable regions. The frequency of occurrence of fragments of like size between populations was used to develop a measure of genetic relatedness.

Relationships among 135 alfalfa accessions were investigated with **principal component** and cluster analyses, based on the genetic distance measures. Distinct clusters were taken as an indication of genetically distinct lineages. The populations investigated represented collections from world regions defined as the centers of origin of specific alfalfa germplasm sources, or else represented collections of introduced, and naturally adapted, accessions from agriculturally advanced regions. In general, this analysis indicated that the accessions from regions of origin of germplasm sources were largely homogeneous, while accessions from areas of introduction were much more diverse. In some cases, the accessions from a region of origin formed distinct clusters, suggesting that divergence has resulted in genetically distinct lines persisting in the original region of origin. Investigation of the stability of the marker fragments through vegetatively, and sexually, propagated plants indicated stable transmission through the sexual phase. However, one of the two regions underwent a deletion of 145 bp of one copy of a tandemly repeated 146 bp region in the equivalent of 80 years of vegetative growth.

L4 ANSWER 5 OF 51 MEDLINE on STN DUPLICATE 3
AN 2000259437 MEDLINE
DN PubMed ID: 10797298
TI Classification of human ovarian tumors using multivariate data analysis of polypeptide expression patterns.
AU Alaiya A A; Franzen B; Hagman A; Silfversward C; Moberger B; Linder S; Auer G
CS Unit of Cell and Molecular Analysis, Department of Oncology and Pathology, Karolinska Institute and Hospital, Stockholm, Sweden..
Alaiya.Ayodele@cck.ki.se
SO International journal of cancer. Journal international du cancer, **(2000 Jun 1)** 86 (5) 731-6.
Journal code: 0042124. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006
ED Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000608
AB Large amounts of data on quantitative **gene expression** are generated by procedures such as 2-DE analysis of proteins or cDNA microarrays. Quantitative molecular variation may potentially be used for the development of methods for the classification of tumors. We used here the statistical concepts of **principal components** analysis (PCA) and partial least square analysis (PLS) in an attempt to type ovarian tumors. Using a set of 170 polypeptides, 22 tumors were used to establish a model ("learning set") for classification into 3 groups (benign/borderline/malignant). Eighteen tumors were then used to test the model. Six of 8 carcinomas and 3 of 4 borderline tumors were correctly classified. Two of 6 benign lesions were correctly classified, 3 were classified as borderline and 1 as carcinoma. We conclude that it may be possible to classify tumors according to their constitutive protein expression profile using multivariate analysis, thus making classification by artificial intelligence a future possibility.
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L4 ANSWER 6 OF 51 MEDLINE on STN
AN 2000410548 MEDLINE
DN PubMed ID: 10902193
TI **Principal components** analysis to summarize microarray experiments: application to sporulation time series.

AU Raychaudhuri S; Stuart J M; Altman R B
CS Stanford Medical Informatics, Stanford University, CA 94305-5479, USA.. sxr@smi.stanford.edu
NC GM-07365 (NIGMS)
LM-07033 (NLM)
LM06244 (NLM)
SO Pacific Symposium on Biocomputing. Pacific Symposium on Biocomputing, **(2000)** 455-66.
Journal code: 9711271.
CY Singapore
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000829
AB A series of microarray experiments produces observations of differential expression for thousands of genes across multiple conditions. It is often not clear whether a set of experiments are measuring fundamentally different **gene expression** states or are measuring similar states created through different mechanisms. It is useful, therefore, to define a core set of independent features for the expression states that allow them to be compared directly. **Principal components** analysis (PCA) is a statistical technique for determining the key variables in a multidimensional data set that explain the differences in the observations, and can be used to simplify the analysis and visualization of multidimensional data sets. We show that application of PCA to expression data (where the experimental conditions are the variables, and the **gene expression** measurements are the observations) allows us to summarize the ways in which gene responses vary under different conditions. Examination of the components also provides insight into the underlying factors that are measured in the experiments. We applied PCA to the publicly released yeast sporulation data set (Chu et al. 1998). In that work, 7 different measurements of **gene expression** were made over time. PCA on the time-points suggests that much of the observed variability in the experiment can be summarized in just 2 components--i.e. 2 variables capture most of the information. These components appear to represent (1) overall induction level and (2) change in induction level over time. We also examined the clusters proposed in the original paper, and show how they are manifested in **principal component** space. Our results are available on the internet at http: www.smi.stanford.edu/project/helix/PCArray .

L4 ANSWER 7 OF 51 MEDLINE on STN DUPLICATE 4
AN 2001186706 MEDLINE
DN PubMed ID: 11274896
TI Genomics and proteomics: the new millennium of drug discovery and development.
CM Erratum in: J Pharmacol Toxicol Methods 2001 Jan-Feb;45(1):85
AU Cunningham M J
CS Genometrix, Inc., 2700 Research Forest Drive, The Woodlands, TX 77381, USA.. mcunningham@genometrix.com
SO Journal of pharmacological and toxicological methods, **(2000 Jul-Aug)** 44 (1) 291-300. Ref: 120
Journal code: 9206091. ISSN: 1056-8719.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English

FS Priority Journals
EM 200105
ED Entered STN: 20010521
Last Updated on STN: 20011105
Entered Medline: 20010517
AB One of the most pressing issues facing the pharmaceutical and biotechnology industry is the tremendous dropout rate of lead drug candidates. Over the last two decades, several new genomic technologies have been developed in hopes of addressing the issues of target identification and lead candidate optimization. **Gene expression** microarray is one of these technologies and this review describes the four main formats, which are currently available: (a) cDNA; (b) oligonucleotide; (c) electrokinetic; and (d) fiberoptic. Many of these formats have been developed with the goal of screening large numbers of genes. Recently, a high-throughput array format has been developed where a large number of samples can be assayed using arrays in parallel. In addition, focusing on **gene expression** may be only one avenue in preventing lead candidate failure. Proteomics or the study of protein expression may also play a role. Two-dimensional polyacrylamide gel electrophoresis (2-DE) coupled with mass spectroscopy has been the most widely accepted format to study protein expression. However, protein microarrays are now being developed and modified to a high-throughput screening format. Examples of several gene and protein expression studies as they apply to drug discovery and development are reviewed. These studies often result in large data sets. Examples of how several statistical methods (**principal components** analysis [PCA], clustering methods, Shannon entropy, etc.) have been applied to these data sets are also described. These newer genomic and proteomic technologies and their analysis and visualization methods have the potential to make the drug discovery and development process less costly and more efficient by aiding to select better target and lead candidates.

L4 ANSWER 8 OF 51 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:478916 BIOSIS
DN PREV200000478916
TI Hierarchical agglomerative nesting of **gene expression** levels from cDNA microarrays.
AU Peterson, Leif E. [Reprint author]
CS Department of Medicine, Baylor College of Medicine, Houston, TX, USA
SO Genetic Epidemiology, (October, 2000) Vol. 19, No. 3, pp. 269. print.
Meeting Info.: Ninth Annual Meeting of the International Genetic Epidemiology Society. San Antonio, Texas, USA. October 27-28, 2000.
ISSN: 0741-0395.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 8 Nov 2000
Last Updated on STN: 10 Jan 2002

L4 ANSWER 9 OF 51 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:149733 BIOSIS
DN PREV200100149733
TI Genetic diversity of Chinese and Japanese Rapeseed (Brassica napus L.) varieties detected by RAPD markers.
AU Ma, Chaozhi; Kimura, Yusuke; Fujimoto, Hideya; Sakai, Takako [Reprint author]; Imamura, Jun; Fu, Tingdong
CS Plantech Research Institute, 1000 Kamoshida, Aoba-ku, Yokohama, Kanagawa, 227-0033, Japan
sakai@rc.m-kagaku.co.jp
SO Breeding Science, (December, 2000) Vol. 50, No. 4, pp. 257-265. print.
ISSN: 1344-7610.